

Short Communication

Narrow spectrum of cross-sensitization with pyridine derivatives

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We have previously reported the occurrence of allergic contact dermatitis from pyridine, 2-vinylpyridine, 4-vinylpyridine and 4-ethylpyridine in a chemist (1). Of the 5 controls who participated in this investigation, 4 became actively sensitized to 1 or more pyridine derivatives. To illuminate their cross-reaction spectrum, we submitted the 5 pyridine-derivatives-sensitized individuals to additional patch tests with an extended series of chemicals that included pyridine, pyridazine, pyrimidine and pyrazine compounds (Fig. 1). Some of these substances were

bought from Aldrich Chemicals while others were obtained from the pharmaceutical industry. Various dilutions were prepared and patch tests were conducted in the usual manner. No positive reaction was seen at day 4 (D4) or later (Table 1).

Comment

Despite the widespread use of pyridine derivatives in chemistry laboratories, the number of reported cases of allergic contact dermatitis from these compounds remains small (1–3). All cases have been occupational, including a worker in a pharmaceutical plant who was sensitized to diaminopyridine (4), and a laboratory technician allergic to pyridine in Karl-Fischer reagent (5).

Patients sensitized to pyridine derivatives have occasionally shown cross-reactions with nicotinic acid (6) or nicotinates (7). Allergic contact dermatitis has been described from zinc pyrithione (8–12) and pyridoxine (13–15), 2 compounds built around a pyridine nucleus. We have included in our testing series miscellaneous systemic drugs that share a pyridine ring, because we were concerned about the risk of systemic contact dermatitis from exposure to these medicaments in sensitized individuals.

Cross-reactivity between pyridine and pyrimidine has not been found (5). However, substituted pyrimidine analogues are known sensitizers, and contact dermatitis has occurred after topical use of 5-fluorouracil (16–18) and idoxuridine (19). Amon et al. (19) have clearly shown that the pyrimidine ring is the allergenic site and that cross-reactivity depends upon substitution in the 5-carbon position with the halogens iodine, bromine or chlorine, but not fluorine. Our study has failed to disclose cross-sensitization to pyrimidine derivatives, including silver sulfadiazine, a topical sulfonamide used extensively in the treatment of burns.

Likewise, no cross-sensitization was detected to pyridazine and pyrazine derivatives, despite certain structural similarity between these chemicals. It thus appears that the cross-reactivity spectrum between these substances is narrow, even though individually they may be strong

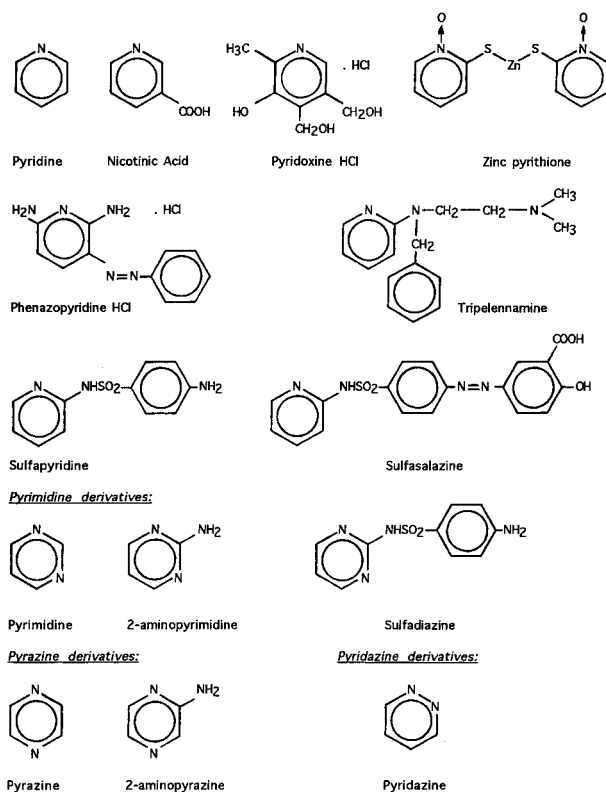


Fig. 1. Chemical structure of pyridine, pyrimidine, pyrazine and pyridazine compounds.

Table 1. Results of patch testing

Test substance	Concentration % (w/vol)	Vehicle	Patients (reading at D4)				
			1	2	3	4	5
<i>Pyridine derivatives</i>							
2-aminopyridine	0.5, 0.1, 0.01	IPA*	—	—	—	—	—
2,6-diaminopyridine	0.5, 0.1, 0.01	IPA	—	—	—	—	—
2,3-diaminopyridine	0.5, 0.1, 0.01	IPA	—	—	—	—	—
3-pyridine carboxylic acid (nicotinic acid)	1.0	aq.	—	—	—	—	—
5-hydroxy-6-methyl-3,4-pyridinemethanol HCl (pyridoxine)	10.0	pet.	—	—	—	—	—
zinc bis (pyridinethiol-1-oxide) (zinc pyrithione)	1.0	pet.	—	—	—	—	—
2,6-diamino-3-phenylazopyridine (phenazopyridine)	5.0	pet.	—	—	—	—	—
2-[benzyl(2-dimethylaminoethyl) amino]pyridine (tripelennamine)	2.5	pet.	—	—	—	—	—
N'-2-pyridylsulfanilamide (sulfapyridine)	5.0	pet.	—	—	—	—	—
5-[p-(2-pyridylsulfamoyl)phenylazo]salicylic acid (sulfasalazine)	5.0	pet.	—	—	—	—	—
<i>Pyrimidine derivatives</i>							
pyrimidine	0.5, 0.1, 0.01	IPA	—	—	—	—	—
2-aminopyrimidine	0.5, 0.1, 0.01	IPA	—	—	—	—	—
2-sulfanilamidopyrimidine Ag (silver sulfadiazine)	1.0	pet.	—	—	—	—	—
<i>Pyrazine derivatives</i>							
pyrazine	0.5, 0.1, 0.01	IPA	—	—	—	—	—
2-aminopyrazine	0.5, 0.1, 0.01	IPA	—	—	—	—	—
<i>Pyridazine derivatives</i>							
pyridazine	0.5, 0.1, 0.01	IPA	—	—	—	—	—

*IPA: isopropyl alcohol.

sensitizers. Minor substitutions in or around the central ring effectively prevent cross-sensitization.

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